Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

CHEST 2021
ANNUAL MEETING | OCTOBER 17-20

Chest Infections

TOPIC: Chest Infections
TYPE: Medical Student/Resident Case Reports

LERONLIMAB AND THE ROLE OF CCR5 SUPRESSION IN COVID-19 TREATMENT

SARAH BJORK AND RUTH MINKIN

INTRODUCTION: Mortality in COVID19 is due to the overwhelming immune response and cytokine storm, leading to acute respiratory distress syndrome (ARDS) and multiorgan failure. Leronlimab, a humanized IgG4,κ monoclonal antibody to C-C chemokine receptor type 5 (CCR5), is under development as a therapy for human immunodeficiency virus (HIV) infection. CCR5 plays a role in the induction of cellular immunity cascade1 and has been studied as a central gene in immune response2,3.

CASE PRESENTATION: 38 year old female with no medical history presented in April 2020 with one week of cough, chest discomfort, and shortness of breath. She tested positive for Sars-CoV-2 and completed 3 days of Plaquenil. On presentation, her oxygen saturation on room air was 93% at rest, 88% with exertion. She was treated with oxygen at 2 L/min via nasal cannula, methylprednisolone, apixiban, ceftriaxone, and doxycycline. Over 48 hours she worsened requiring high-flow oxygen at 25 L/min at 100% with continued rise in ESR, CRP, ferritin, D-dimer. On day 3 of admission, she received one dose of Leronlimab. Within 24 hours inflammatory markers and supplemental oxygen requirements began to lessen. She was discharged on day 10 with supplemental oxygen after a second dose of Leronlimab. Two weeks later, supplemental oxygen was no longer required at rest or with exercise.

DISCUSSION: CCR5 is a β-chemokine receptor similar to the G-protein coupled receptors on the cellular membrane of T-cells and macrophages. CCR5 induces a cellular immunity cascade (CCL5/RANTES) independent of chemotactic cascades1 and thought to increase the leukocyte response to an invading pathogen. Studies are currently ongoing to determine if a pharmaceutical target against a genetic component of the immune and inflammatory response can be identified to stop the over-activation in COVID19. Ray et al identified upregulations of CCR1, 2, and 5 during cytokine over-response postulating a direct connection with sensory neuron activation in the lung that leads to the development of ARDS2.A study by Patterson et al discovered elevated IL-6 and CCL5/RANTES with decreased CD8 T-cell levels in critically ill COVID19 patients. In these patients, Leronlimab led to rapid reduction of IL-6, normalization in CD4/CD8 ratios and a decrease in SARS-CoV-2 levels3.

CONCLUSIONS: In our patient, the use of Leronlimab reduced inflammatory markers and possibly prevented the progression into cytokine storm-mediated multiorgan failure.

REFERENCE #1: Lopalco, Lucia. "CCR5: From Natural Resistance to a New Anti-HIV Strategy." Viruses vol. 2,2 (2010): 574-600. doi:10.3390/v2020574

REFERENCE #2: Ray, Pradipta R et al. "A pharmacological interactome between COVID-19 patient samples and human sensory neurons reveals potential drivers of neurogenic pulmonary dysfunction." Brain, behavior, and immunity vol. 89 (2020): 559-568. doi:10.1016/j.bbi.2020.05.078

REFERENCE #3: Patterson, Bruce K, et al. "Disruption of the CCL5/RANTES-CCR5 Pathway Restores Immune Homeostasis and Reduces Plasma Viral Load in Critical COVID-19." MedRxiv, Cold Spring Harbor Laboratory Press, 1 Jan. 2020.

DISCLOSURES: No relevant relationships by Sarah Bjork, source=Web Response

No relevant relationships by Ruth Minkin, source=Web Response

DOI: https://doi.org/10.1016/j.chest.2021.07.445